UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/994,185 | 11/26/2001 | Mark Leslie White | 27129/33783B | 9922 |

4743 7590 11/12/2004

MARSHALL, GERSTEIN & BORUN LLP
6300 SEARS TOWER
233 S. WACKER DRIVE
CHICAGO, IL 60606

| EXAMINER | |
|---|---|
| CANELLA, KAREN A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | |

DATE MAILED: 11/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/994,185 | WHITE ET AL. | |
| | Examiner | Art Unit | |
| | Karen A Canella | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date Mar 5, 2002.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Acknowledgment is made of applicant's election of the species of Crohn's disease. After search of the prior art, the species election of the Paper mailed June 25, 2004, is withdrawn.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention..

3. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The method of claim 1 fails to correlated the concentration of the lipopolysaccharide binding protein and the standard indicative of exposure to endotoxin with the method objective of determining the exposure of a subject to endotoxin.

Claim 1 recites "standard indicative of the exposure of endotoxin" but fails to provide a limiting definition which would sets the metes and bounds of such a standard.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method wherein the concentration of lipopolysaccharide binding protein in a concentration of greater than 15 ug/ml in human plasma or serum is indicative of a subject suffering from exposure to endotoxin and a method where the concetrations of LBP in human plasma is above the level of the standard values given in Figure 2 for patients having underlying pathologies of pregnancy, graft versus host disease, CLL, cutaneous T cell lymphoma, type I diabetes, aplastic anemia, , Crohn's disease, psoriasis, rheumatoid arthritis,

scleroderma, lupus erythematosus and AIDS, does not reasonably provide enablement for a method wherein the concentration of LBP in a sample of body fluid from a subject is correlated with a standard indicative of the exposure to endotoxin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A requirement of 112, first paragraph is that one of skill in the art should upon reading of the specification be able to make and use a claimed invention without undue experimentation. The instant claims are dependent upon the existence of a standard indicative of exposure to endotoxin in any body fluid, and includes human and non-humans as well as subjects having particular pathological states such as those listed in claims 5-17. It is noted that the claims are not limited to human subjects, nor are the claims limited to bodily fluids such as plasma or serum. The specification states on page 4 lines 6-8 that the invention provides methods for screening for exposure to gram-negative bacterial endotoxin in an acute phase response in humans by assaying for LBP. The specification further states that the standard can include a subjective standard for a given subject determined by LBP levels of that subject in a pre-treatment state such as prior to undergoing surgery (page 4, lines 11-13). The specification states that where access to pretreatment standard level of LBP is not available for a given individual, objective standards based upon population or subpopulation averages may be applied by comparison (page 4, lines 15-17). The specification states that alternative standards could be established depending upon the desired sensitivity and selectivity of an assay method and upon the subpopulation in which a given subject falls, and that standards might be established at different levels for different ages, genders, ethnicities and underlying health conditions of various subpopulations (page 4, lines 22-26). Thus, it is clear that the underlying health conditions of pregnancy, graft versus host disease, CLL, cutaneous T cell lymphoma, type I diabetes, aplastic anemia, , Crohn's disease, psoriasis, rheumatoid arthritis, scleroderma, lupus erythematosus and AIDS would each be subject to having their own standard indicative of exposure to endotoxin. The specification further states that standard levels will differ according to the identity of the particular body fluid which is assayed. One of skill in the art would reasonable conclude that not all bodily fluids, such as sputum and urine, would reflect the same level of exposure to endotoxin as plasma or serum. The specification teaches standard values of

LBP in the plasma of human subjects not exposed to endotoxin, wherein the human subjects suffered from the underlying pathological conditions of rheumatoid arthritis, graft vs host disease, acute lymphoblastic leukemia, chronic lymphocytic leukemia, cutanoeus T-cell lymphoma, diabetes, psoriasis, scleroderma, Crohn's disease, anaplastic anemia and systemic lupus erythematosus (Figure 2). The specification dose not provide a standard of LBP for fluids other than plasma, or in subjects other than human, or for individuals having the underlying pathologies of AIDS or pregnancy. Thus, in order to practice the claimed method to the full extent of the claims, one of skill in the art would be required to establish standards of LBP indicative of exposure to endotoxin for individuals with the underlying health disorders of AIDS and pregnancy, at all genders and ages, as well as to establish standards of LBP indicative of exposure to endotoxin in body fluids beyond those of plasma and serum for all of the disorders of rheumatoid arthritis, graft vs host disease, acute lymphoblastic leukemia, chronic lymphocytic leukemia, cutanoeus T-cell lymphoma, diabetes, psoriasis, scleroderma, Crohn's disease, anaplastic anemia, systemic lupus erythematosus, pregnancy and AIDS. Because the determination of a standard requires numerous measurements of both individuals afflicted with exposure to endotoxin and individuals not afflicted by exposure to endotoxin in order to determine the concentration of LBP above which and individual would be exposed to endotoxin, one of skill in the art would be subject to undue experimentation in order to determine a standard for any of a number of bodily fluids in individuals having different underlying pathologies such as those claimed in claims 5-17 and in individuals not having any underlying pathological state.

***Double Patenting***

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims claims 1-11 of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804,367 and claims 1 and 2 of U. S. Patent No.5,484,705. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '618, '367 and '705 anticipate the instant claims 1-4.

8. Claims 1-4 and 11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 of U.S. Patent No. in view of the abstract of Gardener et al (Journal of Reproductive Medicine, 1977, Vol. 19, pp. 64-66). Claim 11 embodies the method of claim 1 wherein the subject has aplastic anemia. The abstract of Gardener teaches that the risk of infection is high in patients undergoing immunosuppression as a result of aplastic anemia. It would have been prima facie obvious at the time the invention was made to use the method of determining the exposure of a subject to endotoxin of the claims of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 on a subject having aplastic anemia. One of skill in the art would have been motivated to do so through the teachings of the abstract of Gardner which identifies individuals having aplastic anemia as susceptible to infections.

9. Claims 1-4 and 12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 of U.S. Patent No. in view of the abstract of Grobler et al (Gut, 1993 Oct, vol. 34, pp. 1384-1388). The abstract of Grobler et al teaches that subjects having Crohn's disease are susceptible to sepsis after surgery. It would have been prima facie obvious at the time the claimed invention was made to use the method of determining the exposure of a subject to endotoxin of the claims of U. S. Patent No.

5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 on subjects having Crohn's disease. One of skill in the art would have been motivated to do so through the teachings of the abstract of Grobler et al which identifies Crohn's disease as a pathology imparting susceptibility to sepsis.

10. Claims 1-4 and 14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 of U.S. Patent No. in view of the abstract of Gelman et al (Radiology, 1977, Vol. 122, pp. 17-23). The abstract of Gelman et al teaches that septic arthritis is a complication of rheumatoid arthritis. It would have been prima facie obvious at the time the claimed invention was made to use the method of determining the exposure of a subject to endotoxin of the claims of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 on subjects having rheumatoid arthritis. One of skill in the art would have been motivated to do so by the teachings of the abstract of Gelman identifying rheumatoid arthritis as a pathology which imparts susceptibility to septic arthritis.

11. Claims 1-4 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 of U.S. Patent No. in view of the abstract of Cohen et al (QJM, 1982, Vol. 51, pp. 1-15). The abstract of Cohen et al identifies systemic lupus erythematosus as a pathology which impart susceptibility to infection. It would have been prima facie obvious at the time the claimed invention was made to use the method of determining the exposure of a subject to endotoxin of the claims of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 on patients having systemic lupus erythematosus. One of skill in the art would have been motivated to do so by the teachings of Cohen et al on the increased susceptibility to infectious complications in patients suffering from systemic lupus erythematosus

12. Claims 1-4 and 17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 of U.S. Patent No. in view of the abstract of Allwright et al (Clinical Nuclear Medicine, 1988, Vol. 13, pp. 506-508). The abstract of Allwright et al teaches that AIDS patients are susceptible to mycobacteria avium-intracellular septicemia. It would have been prima facie obvious at the time the claimed invention was made to use the method of determining the exposure of a subject to endotoxin of the claims of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 on patients having AIDS. One of skill in the art would have been motivated to do so by the teachings of the abstract of Allwright indicating that AIDS patients are susceptible to septicemia.

13. Claims 1-5 and 11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 of U.S. Patent No. in view of the abstract of Hunt (Journal of Immunology, 1989). Hunt teaches that pregnancy losses are often due to infections by gram-negative bacteria within the uteroplacental unit. It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of determining the exposure of a subject to endotoxin of the claims of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 on a pregnant subject. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Hunt on the association of lipopolysaccharide binding protein and endotoxin susceptibility.

14. Claims 1-4 and 10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 of U.S. Patent No. in view of the abstract of Martin (Immunology, 1991, Vol. 73, pp. 123-125)

The abstract of Martin et al teaches that monocyte trafficking is abnormal in recent onset type 1 diabetes.. It would have been prima facie obvious to one of ordinary skill in the art at the

time the claimed invention was made to use the methods of the claims of U. S. Patent No. 5,891,618, claims 1-11 U. S. Patent No.5,804367 and claims 1 and 2 of U. S. Patent No.5,484,705 on a subject having type 1 diabetes.. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of the abstract of Martin on the abnormalities associated with monocytes in subjects having recently acquired type 1 diabetes.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
11/9/2004

Karen A. Canella
KAREN A. CANELLA PH.D
PRIMARY EXAMINER